

Appl. No. 09/489,667  
Reply to Office Action of December 21, 2004

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1-68. (Cancelled)

69. (Currently amended) An agent for treating pain comprising a modified clostridial neurotoxin, wherein the modified clostridial neurotoxin is obtained by removing or modifying an H<sub>c</sub> domain of a native clostridial neurotoxin to form an intermediate clostridial neurotoxin and covalently coupling ~~or recombinantly fusing~~ substance P to the intermediate clostridial neurotoxin so that the modified clostridial neurotoxin no longer binds to neurotoxin receptors at a neuromuscular junction with the same affinity as the native clostridial neurotoxin.

70. (Previously presented) The agent of claim 69 wherein the clostridial neurotoxin is obtained from an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum and Clostridial tetani.

71. (Previously presented) The agent of claim 69 wherein the clostridial neurotoxin is a botulinum toxin selected from the group consisting of serotype A, serotype B, serotype C<sub>1</sub>, serotype D, serotype E, serotype F and serotype G.

72. (Previously presented) The agent of claim 69 wherein the clostridial neurotoxin is botulinum toxin serotype A.

Appl. No. 09/489,667  
Reply to Office Action of December 21, 2004

73. (Previously presented) The agent of claim 69 wherein the clostridial neurotoxin comprises an H<sub>N</sub> and an L chain.

74. (Previously presented) The agent of claim 73 wherein the H<sub>N</sub> is obtained from an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum and Clostridial tetani.

75. (Previously presented) The agent of claim 73 wherein the L chain is obtained from an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.

76. (Previously presented) The agent of claim 73 wherein the H<sub>N</sub> is obtained from a botulinum toxin selected from the group consisting of botulinum toxin serotype A, serotype B, serotype C<sub>1</sub>, serotype D, serotype E, serotype F and serotype G.

77. (Previously presented) An agent for treating pain comprising a botulinum toxin, without an H<sub>C</sub> that binds to receptors at the neuromuscular junction with the same affinity as native botulinum toxin, covalently coupled to substance P.

78. (Previously presented) An agent for treating pain comprising a botulinum toxin serotype A, without a functional H<sub>C</sub> domain, covalently coupled to substance P.

79. (Previously presented) An agent for treating pain comprising a botulinum toxin covalently coupled to substance P, wherein an H<sub>C</sub> of the toxin has been removed.

Appl. No. 09/489,667  
Reply to Office Action of December 21, 2004

80. (Previously presented) An agent for treating pain comprising a botulinum toxin serotype A covalently coupled to substance P, wherein an H<sub>c</sub> of the toxin has been removed, the agent treats pain by acting on a projection neuron.